HeartMate II

Decision Memo for Ventricular Assist Devices as Destination Therapy (CAG-00119R2)

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) is issuing the following decision:

The evidence is adequate to conclude that VAD implantation as destination therapy improves health outcomes and is reasonable and necessary when the device has received FDA approval for a destination therapy indication and only for patients with New York Heart Association (NYHA) Class IV end-stage ventricular heart failure who are not candidates for heart transplant and who meet all of the following conditions:

- a. Have failed to respond to optimal medical management (including beta-blockers, and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump dependent for 7 days, or IV inotrope dependent for 14 days; and,
- b. Have a left ventricular ejection fraction (LVEF) < 25%; and,
- c. Have demonstrated functional limitation with a peak oxygen consumption of ≤ 14 ml/kg/min unless balloon pump or inotrope dependent or physically unable to perform the test.

CMS is not changing any other parts of Section 20.9 "Artificial Hearts and Related Devices" of the National Coverage Determinations Manual. The final policy in its entirety is available in Appendix A with changes appearing in Section 3.

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Decision Memo

To: Administrative File CAG-00119R2

From:

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Subject: Coverage Decision Memorandum for Ventricular Assist Devices as Destination Therapy (VAD)

Date: November 9, 2010

I. Decision

The Centers for Medicare & Medicaid Services (CMS) is issuing the following decision:

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II. Background

Heart failure is a condition in which the heart cannot pump enough blood to the body. The incidence of heart failure rises with advancing age and continues to be a significant cause of morbidity and mortality for elderly Medicare patients. According to the Centers for Disease Control and Prevention (www.cdc.gov/dhdsp/library/fs_heart_failure.htm), in the United States approximately 5.8 million people have heart failure with about 670,000 new cases diagnosed each year. About one in five patients with heart failure will die from the disease within one year of its diagnosis.

While heart failure is not caused by aging, the elderly are more likely to have had predisposing conditions such as long-standing hypertension (high blood pressure) or myocardial infarction (heart attack). Depending on the severity of heart failure, patients can be treated with several different types of drugs, including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), beta-blockers, digoxin, inotropes and others. Inotropes are drugs that increase the contractile force of the heart. These medications cannot reverse heart failure but may improve the symptoms of heart failure by reducing fluid, reducing strain on the heart by reducing blood pressure, slowing heart rate or making the heart beat stronger. Despite improvements in available medications and closer monitoring of patients, heart failure continues to be a progressive disease, which becomes refractory to medical management over time. Advanced or end-stage heart failure can be cured by heart transplant. Unfortunately, elderly patients are not generally candidates for transplants due to age alone or comorbid conditions, which present unacceptable surgical risks. Only about 2300 heart transplants are performed annually in the United States with available organs generally allocated to younger patients most likely to survive surgery and have a prolonged benefit (www.medhelp.org/NIHlib/GF-270.html).

The functional limitations due to heart failure can be quantified using the New York Heart Association (NYHA) classification system, which was most recently updated by the American Heart Association (AHA). In 1994, the Criteria Committee of the New York City affiliate of AHA revised the classification to describe the following functional classes of heart failure (http://www.americanheart.org/presenter.jhtml?identifier=4569):

Class I

Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.

Class II

Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.

Class III

Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.

Class IV

Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

It has been noted in the literature that the NYHA classification system is often subjective with physicians having difficulty assigning patients to any one class. Therefore, in an article published in the American Family Physician (Chavey et al, 2001), the authors offer a classification scheme that they believe will result in less ambiguous patient assignment to a class. The authors present new symptomatic definitions and link them to a corresponding NYHA class or classes. In this scheme, patients with a recent history of dyspnea at rest and patients with dyspnea at rest are assigned to different classes as the authors believe this to be indicative of prognosis.

Asymptomatic – NYHA Class I Symptomatic – NYHA Class II/III Symptomatic with recent history of dyspnea at rest – NYHA Class IIIB Symptomatic with dyspnea at rest – NYHA Class IV

This proposal did not become a standard for clinical heart failure classification.

Ventricular assist devices (VADs) are mechanical pumps used to assist a damaged or weakened heart in pumping blood. These devices support a patient's weakened native heart but do not replace it, unlike heart transplant. VADs are surgically attached to a ventricle of the native heart and the mechanical pump is implanted in the abdomen or in the chest cavity. The device requires a driveline that goes from the pump inside the patient's body to an external power and control unit. Typically these external portions of the device are portable and the patient can carry them in a small bag along with extra batteries. The device also has a base unit that is not portable but can be used when the patient is at home or in the hospital.

Selection criteria for severe heart failure patients who may be considered for VAD implantation include clinical assessment (NYHA functional class, clinical history, management and duration of disease, cardiopulmonary stress testing) and cardiac and anatomic considerations (body size), as well as non-cardiac considerations and assessment of operative risk.

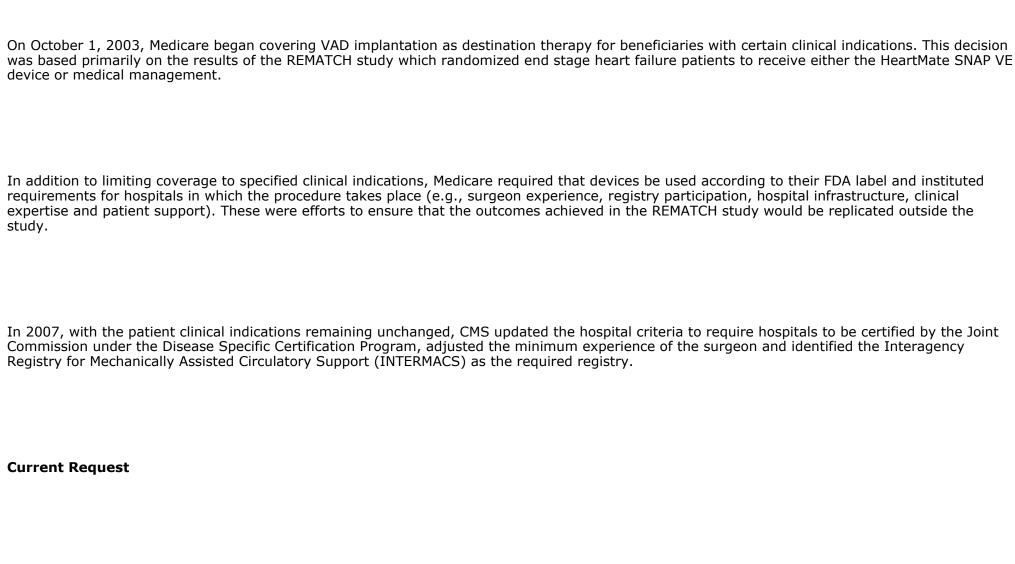
Mechanical circulatory support devices, including VADs, have been used to assist acutely injured hearts to recover from such things as infection or the effects of open heart surgery for a number of years. More recently, VADs have been used to support failing hearts over longer periods of time as a "bridge to transplant" until a suitable donor heart becomes available. Information from the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) states that at any one time 3500 to 4000 patients are listed for heart transplant but more than 25% of these patients may die before a donor heart is found (www.medhelp.org/NIHlib/GF-270.html). With the advent of improvements in the reliability and durability of VADs some patients on transplant waiting lists actually recovered cardiac function and were able to have their devices removed. Still other patients received newer smaller devices, which enabled them to leave the hospital and return home, sometimes for long periods, while awaiting transplant. Even patients with end-stage heart failure who are not transplant candidates have achieved improved survival with permanent VAD support through destination therapy (DT). As the number of patients attaining long-term survival with VADs continues to rise, new research seeks to expand the indications for VAD implantation to include patients in earlier stage heart failure to prevent development of unsurvivable comorbidities which could limit the clinical benefit of a VAD.

In November, 2002, based on the successful completion of the REMATCH clinical trial the FDA expanded the approved indications for a previously approved bridge device (HeartMate™ SNAP VE LVAS) for use by end-stage, non-transplantable patients as permanent or "destination therapy." That approval stated: "This device is now also indicated for use in patients with New York Heart Association Class IV end-stage left ventricular failure who have received optimal medical therapy for at least 60 of the last 90 days, who have a life expectancy of less than two years, and who are not eligible for cardiac transplantation."

On January 20, 2010, a second device (HeartMate II^{IM}) was approved by the FDA as destination therapy "for use in patients with New York Heart Association (NYHA) Class III B or IV end-stage left ventricular failure, who have received optimal medical therapy for at least 45 of the last 60 days and are not candidates for cardiac transplantation." The HeartMate II is a continuous-flow device weighing approximately one pound. It is "implanted below the heart with its entrance attached to the left ventricle and its exit connected to the aorta... Blood flows from the heart into the pump. A small electric motor in the pump drives a rotor inside the pump which pushes blood into the aorta and out to the body. A flexible tube passes through the patient's skin and connects the implanted pump to a small controller worn outside the body. The controller is powered either by batteries or connected by means of a power supply to a standard household electrical power outlet."

(http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm201473.htm)
The patient population on which the new device was studied was more diverse than that in the REMATCH trial, and had somewhat different patient selection criteria than the earlier destination patients.

III. History of Medicare Coverage



CMS received a request from Thoratec, Inc. to reconsider Section 20.9 of the National Coverage Determinations Manual related to VADs used as destination therapy, based on the outcomes of the HeartMate II Destination Therapy study. Specifically, Thoratec requested expanding coverage to include patients with NYHA Class IIIB symptoms, to reduce the required time on optimal medical management to 45 of the last 60 days, to include time on a balloon pump or inotrope therapy as indications for coverage, to increase the peak oxygen consumption to < 14 ml/kg/min and to remove the body size requirement. The request did not include changes to other portions of the NCD (facility criteria, post-cardiotomy or bridge to transplant indications).

CMS is focusing this review on the patient selection aspect of the policy and is not reviewing other portions of the NCD as part this analysis.

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Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category under Part A or Part B as a prerequisite to Medicare coverage. VADs may fall within the Inpatient Hospital Services benefit category (section 1861(b)(2) of the Social Security Act (the Act)), which describes supplies, appliances, and equipment furnished by the hospital, for use in the hospital, for the care and treatment of inpatients. After a VAD has been surgically implanted into the patient and when the patient is not a hospital patient, the replacement of an external part or parts may be covered under Medicare Part B within the Prosthetic Device benefit category (section 1861(s)(8) of the Act). This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

February CMS opens a National Coverage Analysis to reconsider the patient population covered for the implantation of a VAD as destination therapy.

March 24, The initial 30-day public comment period closes. 2010

August 19, CMS posts the proposed decision memorandum and begins a second 30-day public comment period. 2010

September The second 30-day public comment period closes. 18, 2010

V. FDA Status

HeartMate II LVAS

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On January 20, 2010, Thoratec Inc. received FDA approval to expand the labeled indication for the HeartMate II Left Ventricular Assist System to include patients that are not candidates for heart transplantation. The device was approved in 2008 for a bridge to transplant indication. As stated in the FDA approval letter (http://www.accessdata.fda.gov/cdrh_docs/pdf6/P060040S005a.pdf), the device indication is as follows:

This device is indicated for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from non-reversible left ventricular failure. It is now also indicated for use in patients with New York Heart Association (NYHA) Class IIIB or IV end-stage left ventricular failure who have received optimal medical therapy for at least 45 of the last 60 days, and are not candidates for cardiac transplantation. The HeartMate II LVAS is intended for use both inside and outside the hospital, or for transportation of ventricular assist device patients via ground ambulance, fixed-wing aircraft, or helicopter.

HeartMate II is a continuous-flow (non-pulsatile) ventricular assist device that is smaller in size than previously FDA approved devices.

HeartMate XVE LVAS

On April 4, 2003, Thoratec Inc. received FDA approval to expand the labeled indication for the HeartMate XVE to include patients that are not candidates for heart transplant. The device was previously approved for a bridge to transplant indication. As stated in the FDA approval order statement (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pmasimplesearch.cfm?db=pma&id=13984#aostatement), the device indication is as follows:

Approval for an expanded indication for use for the thoratec heartmate xve lvas. This device system is indicated for use as a bridge to cardiac transplantation in cardiac transplant candidates at risk of imminent death from nonreversible left ventricular failure. It is now also indicated for use in patients with new york heart association class iv end stage left ventricular failure who have received optimal medical therapy for at least 60 of the last 90 days, and who have a life expectancy of less than two years, and who are not eligible for cardiac transplantation. The device system is approved for use both inside and outside the hospital.

The HeartMate XVE is a pulsatile device that requires a minimum body surface area of 1.5m² for implantation.

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VI. General Methodological Principles

When making national coverage decisions under section 1862(a)(1)(A) of the Social Security Act, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

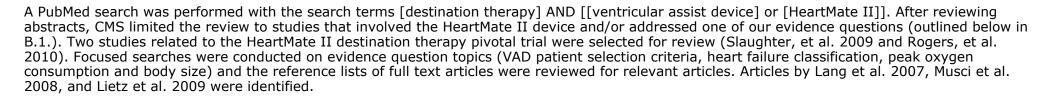
A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix B. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction
Our review focuses on published evidence related to four patient selection criteria from the HeartMate II destination therapy study that Thoratec is requesting be reflected in Medicare coverage. Currently, the HeartMate II study entry criteria and the current destination therapy NCD differ in these areas: 1) heart failure classification, 2) time on optimal medical management, inotropes and balloon pump, 3) peak oxygen consumption, and 4) body surface area (BSA).
In this coverage analysis, we considered destination therapy studies and evidence that were published since the last reconsideration in 2007. It incorporates all evidence from prior decision memoranda regarding this issue. A summary of the body of evidence reviewed to date in developing this decision memorandum is available via the final decision memoranda released following the completion of each of the prior national coverage analyse (NCAs) for reconsiderations of the artificial heart and related devices NCD (http://www.cms.gov/mcd/viewdecisionmemo.asp?id=79 and http://www.cms.gov/mcd/viewdecisionmemo.asp?id=187).
The significant outcomes of interest related to VAD implantation are all-cause mortality, quality of life and adverse events. As discussed in the decision memorandum from 2003 when the REMATCH study was evaluated, an advantage in mortality as the result of this or any other therapy, however, must be weighed against the likelihood of adverse events or other negative consequences associated with its use, such as infection, prolonged hospitalization, or increased bleeding. In addition to these outcomes of interest, we are focusing on information related to patient selection criteria so patients can be appropriately and carefully selected for the procedure.

Literature Search



In addition, CMS located the published FDA Summary of Safety and Effectiveness and includes that document in the body of evidence. The Summary of Safety and Effectiveness was located by searching the FDA website (www.fda.gov) using the search terms [HeartMateII] AND [destination therapy].

Searches of PubMed using the search terms [NYHA classification iiib, IIIB, iiib/iv and IIIB/IV] did not result in locating an accepted standard definition of NYHA Class IIIB heart failure.

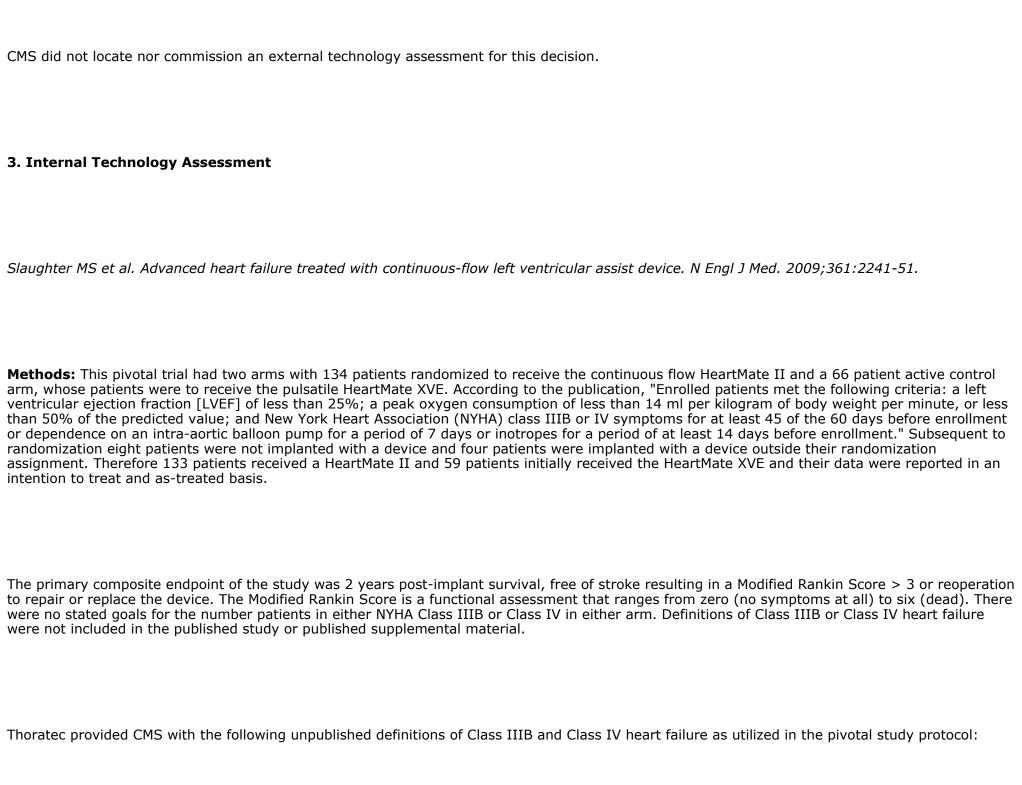
B. Discussion of evidence reviewed

1. Question

Is the evidence adequate to conclude that VADs improve health outcomes of Medicare beneficiaries who are not candidates for transplant and who:

- a. are said to have NYHA Class IIIB symptoms?
- b. have failed to respond to optimal medical management (including beta-blockers, and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or patient is balloon pump dependent for 7 days, or IV inotrope dependent for 14 days?
- c. have demonstrated functional limitation with a peak oxygen consumption of ≤ 14 ml/kg/min if not contra-indicated?
- d. have a body surface area of $<1.5m^2$?

2. External Technology Assessment



NYHA Class IIIB:

Cardiac disease resulting in marked limitations of physical activity. Patients are comfortable at rest. Mild physical activity causes fatigue, palpitation, dyspnea, or anginal pain.

NYHA Class IV:

Cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the angina syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Results: The patients in both arms had similar baseline characteristics (Table 1):

Table 1: Baseline characteristics of the study patients, according to treatment group (Slaughter et al., 2009).

Characteristic	HeartMate II	HeartMate XVE
Age—yr.		
Mean	62 ± 12	63 ± 12
Median(range)	64(26-79)	65 (29-81)
Male sex—no. (%)	108 (81)	61 (92)
LVEF	17.0 ± 5.5	16.8 ± 5.4
Ischemic heart failure—no. (%)	88 (66)	45 (68)
Intravenous inotrope—no.(%)	103 (77)	55 (83)
Biventricular pacemaker	85(63)	39 (59)
ICD	111(83)	52 (79)
Intra-aortic balloon pump	30(22)	15(23)
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Characteristic HeartMate XVE

Among the 181 patients assessed for NYHA class at baseline, 5 were class IIIA (undefined in the study), 38 were class IIIB, and 138 were class IV. Neither the published study nor the published supplement accompanying it gave any breakdown by NYHA class of the patient characteristics or outcomes.

The primary endpoint (2-year post implant survival free of stroke) of the pivotal study reported on an intent to treat basis was met by 62 of the 134 patients (46%) in the continuous-flow device arm and 7 of the 66 patients (11%) the pulsatile device arm. The first occurring reason for failing to achieve the composite endpoint in the HeartMate II trial differed by device (Table 2).

Table 2. Primary endpoint according to treatment group (Slaughter, et al. 2009):

	HeartMate II	HeartMate XVE	P Value
Stroke (Rankin score > 3)	15(11%)	8 (12%)	0.56
Reoperation (pump/repair replace)	13 (10%)	24(24%)	< 0.001
Death within 2 yrs of implantation	44 (33%)	27(41%)	0.048
Any (primary endpoint)	72(54%)	59 (89%)	< 0.001

Table 3. Functional status and quality of life, reported on an as-treated basis, according to time since device implant (Slaughter et al., 2009).

	Baseline	ЗМо	12Mo	24Mo
NYHA class				
No.of patients tested (no./%)	126	91	72	50
Class I	0	30 (33)	30 (42)	21 (42)
Class II	0	38 (42)	25 (35)	19 (38)

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	Baseline	ЗМо	12Mo	24Mo
Class IIIA	4 (3)	16 (18)	13 (18)	6 (12)
Class IIIB	27 (21)	5 (5)	4 (6)	1 (2)
Class IV	95 (75)	2 (2)	0	3 (6)
Six Minute walk				
No. patients tested	50	77	61	36
Distance meters	182 ± 140	319 ± 191	318 ± 164	377 ± 191
Minnessota Living with Heart failure questionnaire				
No. patients tested	116	89	76	44
Score	75.4 ± 17.7	37.4 ± 22.2	34.1 ± 22.4	29.6 ± 22.4
Kansas City Cardiomyopathy questionnaire				
No. patients tested	115	89	76	47
Overall summary score	27.4±16.3	63.4 ± 18.5	65.9 ± 20.0	69.9 ± 18.7
Clinical summary score	35.1±18.5	47.2 ± 17.4	68.6 ± 21.8	72.9 ± 19.3

Data on functional status and quality of life for patients who received the pulsatile device demonstrate improvements over time (Table 3). We have not reproduced the data for the pulsatile device as it is not the subject of this decision. The entire table is included in the published article.

Adverse events and associated relative risks were reported on an as treated basis with results for the continuous-flow device patients showing lower risk in all measures (not all were statistically significant). Lowered risk reached statistical significance for pump replacement, sepsis, medical management (with inotropes) of right heart failure, respiratory failure and renal failure. While continuous-flow patients demonstrated lower risk, their absolute adverse event rates are important to note. Of the continuous-flow patients, 35% experienced an VAD related infection, 36% had sepsis, 16% had renal failure and 30% had bleeding requiring surgery and 18% had a stroke.

Authors' Conclusions: The investigators concluded that the "study shows improvements in the rate of survival, quality of life, functional capacity of patients, and device durability with the continuous-flow...device as compared to the pulsatile-flow...device" and support its use "to provide long-term hemodynamic support that is linked to improvements in longevity and quality of life."

FDA Summary of Safety and Effectiveness. PMA number P060040/S005. January 10, 2010.

This document describes the evidence considered by FDA in evaluating the HeartMate (HM) II for destination therapy. A central consideration is the pivotal trial which compared the HeartMate XVE to the HeartMate II for use in destination therapy, reported by Slaughter et al, 2009. but with independent FDA data analysis. Effectiveness of the HM II was evaluated using a composite endpoint including survival at 2 years, free of stroke resulting in a Modified Rankin Score > 3 or reoperation to repair or replace the device. Safety was documented by incidence of adverse events and device malfunctions and failures compared to the XVE. Secondary objectives evaluated included separate evaluations of each component of the endpoint, functional status (6-minute walk, patient activity score, and NYHA class), health status including quality of life (Minnesota Living with Heart Failure and Kansas City Cardiomyopathy Questionnaire), all adverse events, re-operations, re-hospitalizations, and neurocognative assessments (memory, language, visual/spatial perception, processing speed and abstract/executive function).

Methods:The study design was a prospective, randomized, unblinded, non-inferiority evaluation of HM II in end-stage left ventricular failure patients who were not candidates for heart transplant and were refractory to optimal medical therapy. The protocol's analysis plan specified testing for superiority once non-inferiority was established. Two patients were randomized to HM II for every patient randomized to XVE. Randomization was stratified by study center and blocked to maintain the 2:1 ratio over time. Two hundred patients were enrolled into the Primary Cohort (134 HM II and 66 XVE) at 38 sites from March 2005 to May 2007. All 200 patients in the Primary Cohort were followed for at least two years.

Four additional cohorts were considered by FDA in their evaluation:

- Small BSA Cohort: 24 patients with BSA < 1.5m² who could not be randomized to XVE due to its size.
- XVE Exchange Cohort: 123 failed XVE patients who received HM II as a replacement.
- Randomized Continued Access Protocol (CAP) Cohort: 187 patients enrolled under the primary cohort protocol after the primary cohort had been filled.
- Anatomic Deviation Cohort: 99 patients with BSA > 1.5m² who could not be randomized to XVE due to body habitus or other anatomic considerations.

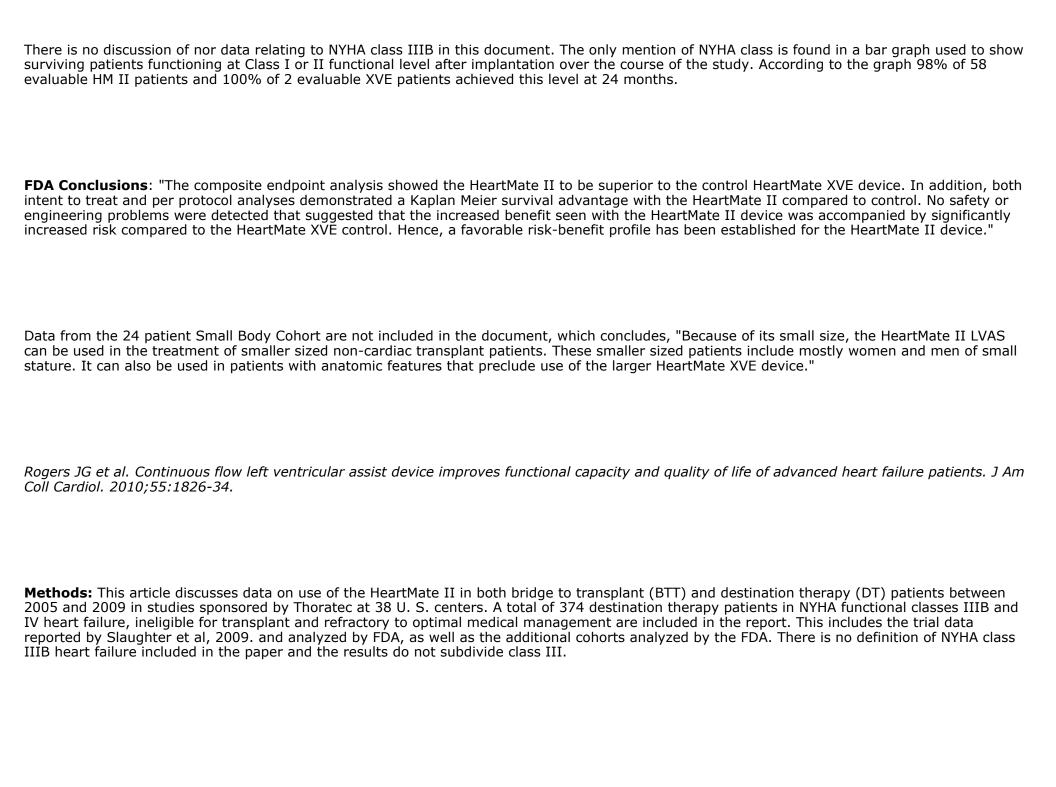
Patients meeting the study endpoint were considered a success and a failure if not. Patients urgently transplanted due to device failure were study failures. Patients electively transplanted after reversal of a pre-enrollment co-morbidity were followed and considered a success if they ultimately achieved the composite endpoint within 2 years of VAD implant.

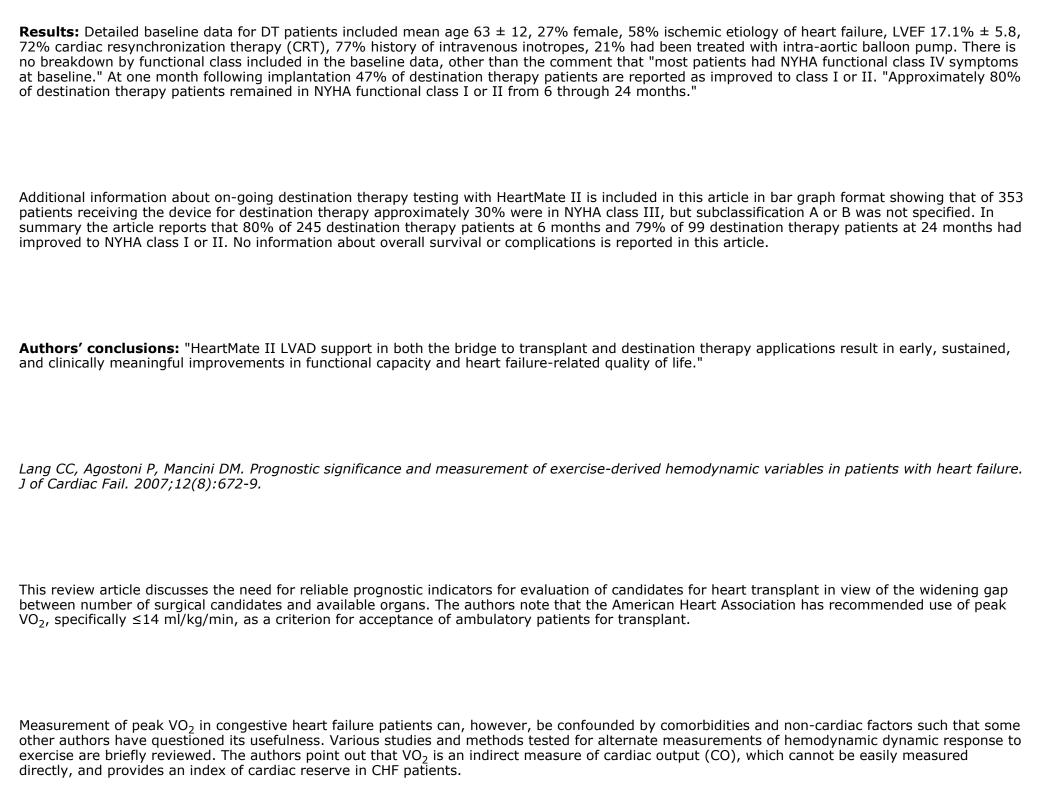
Results:Reasons for patient ineligibility for transplant included age (28%), recent cancer history (9%), obesity (7%), and substance abuse or insufficient social support (7%). Patient age range 26 to 81 yrs, median 64 yrs. No significant differences in age, BSA, body mass index (BMI), etiology or ethnicity between HM II and XVE groups. HM II group contained 19% females and XVE 8%, but, overall, males with ischemic disease predominated. Notable in patient history: 83% of patients entered the study with ICDs and 16% had a history of stroke; 79% of patients on inotrophs at baseline; 23% on intra-aortic balloon pump; and 8% on mechanical ventilation (indications of end-stage heart failure).

Table 4: As treated analysis of patient survival at 2 years by original implanted device. 62/134 HM II (46%) and 7/66 XVE (11%) patients achieved the composite endpoint:

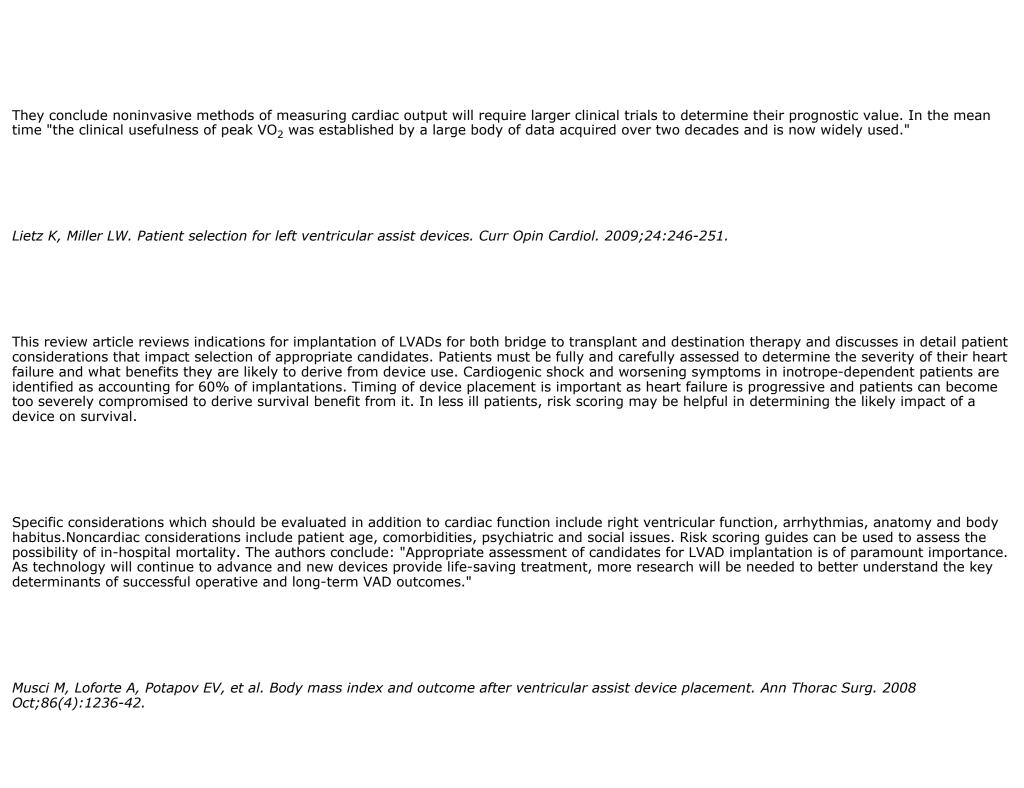
		HM II (n 133)	XVE (n 59)
Ongoing on original device		50(38%)	0 (0%)
Ongoing with replacement same type device		12 (9%)	2 (3%)
Ongoing with replacement alternate type device		0 (0%)	14 (24%)
Transplanted		13(10%)	8 (19%)
Explanted for recovery		1(1%)	1 (1%)
	Total	76 (57%)	25 (42%)

The primary causes of death of the 57 HM II patients were: Stroke—13 pts (10%); right heart failure—8 pts (6%); device malfunction (loss of power, device thrombosis, VAD dysfunction)—10 pts (8%). In 34 XVE patients causes of death were: Stroke –11 pts (19%); right heart failure –5 pts (8%); infection—6 pts (10%); multi-system organ failure—4 pts (7%).





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Methods: A retrospective analysis of 590 consecutive patients with advanced heart failure who underwent VAD placement between 1996 and 2006 at Berlin. Patients were divided into five groups based on body-mass index (BMI, kg/m2) (< 20; 20-24; 25-29; 30-35; and > 35). Twenty patients comprised the group with BMI < 20. In a multivariate analysis adjusted for age, sex, diagnosis, emergency level, and type of device (left ventricular or biventricular assist device), procedural success (recovery, transplantation, or 30-day survival) and complications were analyzed. The best group was set as reference category for calculation of odds ratios.
Results: The groups with both extremes of BMI had the worst outcomes. The best procedural success was in the group with BMI 25 to 29 kg/m². Underweight patients had similar survival rates to patients with normal weight. The unadjusted odds ratio of 30-day mortality for BMI < 20 kg/m² was 2.1 (95% confidence interval 0.9-4.7, p = .05) compared with the 25-29 BMI group. Overweight and obese patients did not have decreased survival. Extreme obesity at the time of VAD implantation showed elevated risk for postoperative death. There was no significant difference for BMI groups in the type of complications and cause of death. Cumulative survival curves for BMI category and overall VAD patient survival showed no significant differences in cause of death by BMI group.
Authors' Conclusions: "Cardiac cachexia [muscle wasting and general debility that can occur during a chronic disease] need not be an exclusion criterion for VAD placement. Underweight patients appear to have benefit from mechanical support. Severely obese patients should be carefully selected before VAD placement."
4. MEDCAC
A meeting of the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) was not convened for this analysis.

5. Evidence-based guidelines

Evidence-based guidelines regarding the use of mechanically assisted circulatory support were not located. CMS also searched for guidelines regarding the treatment of heart failure and heart failure classification systems; one guideline and one guideline update was located.

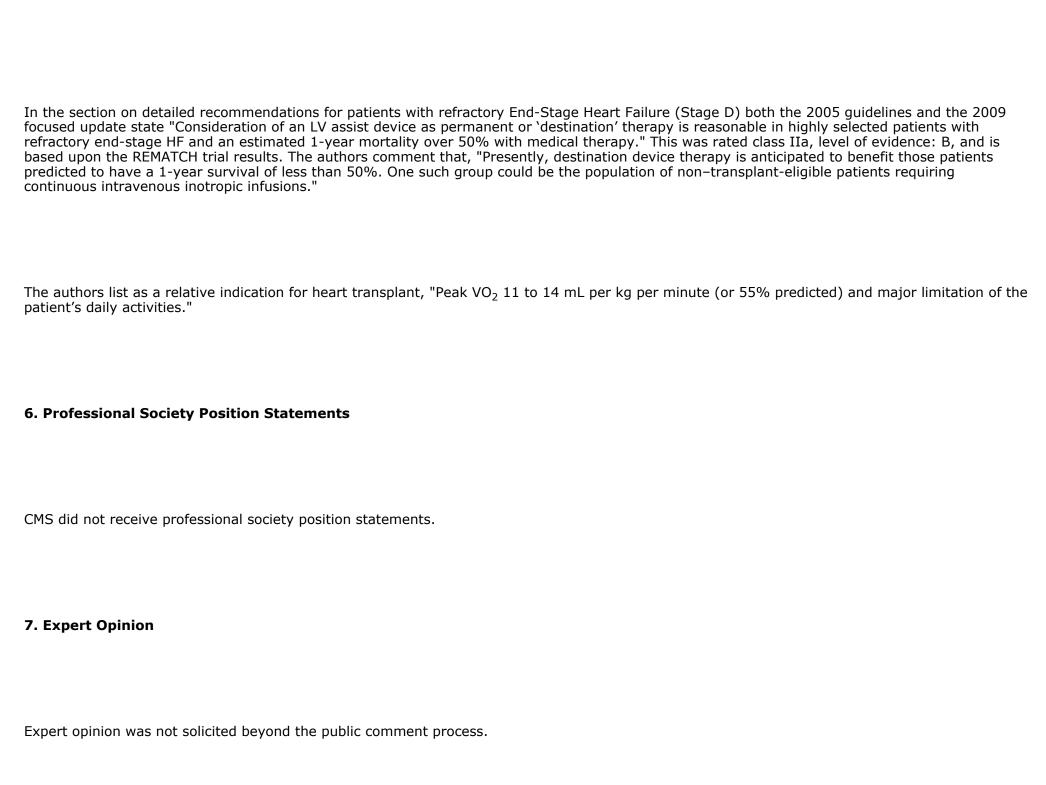
Hunt SA et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). American College of Cardiology Web Site. Available at: http://www.acc.org/clinical/guidelines/failure/index.pdf.

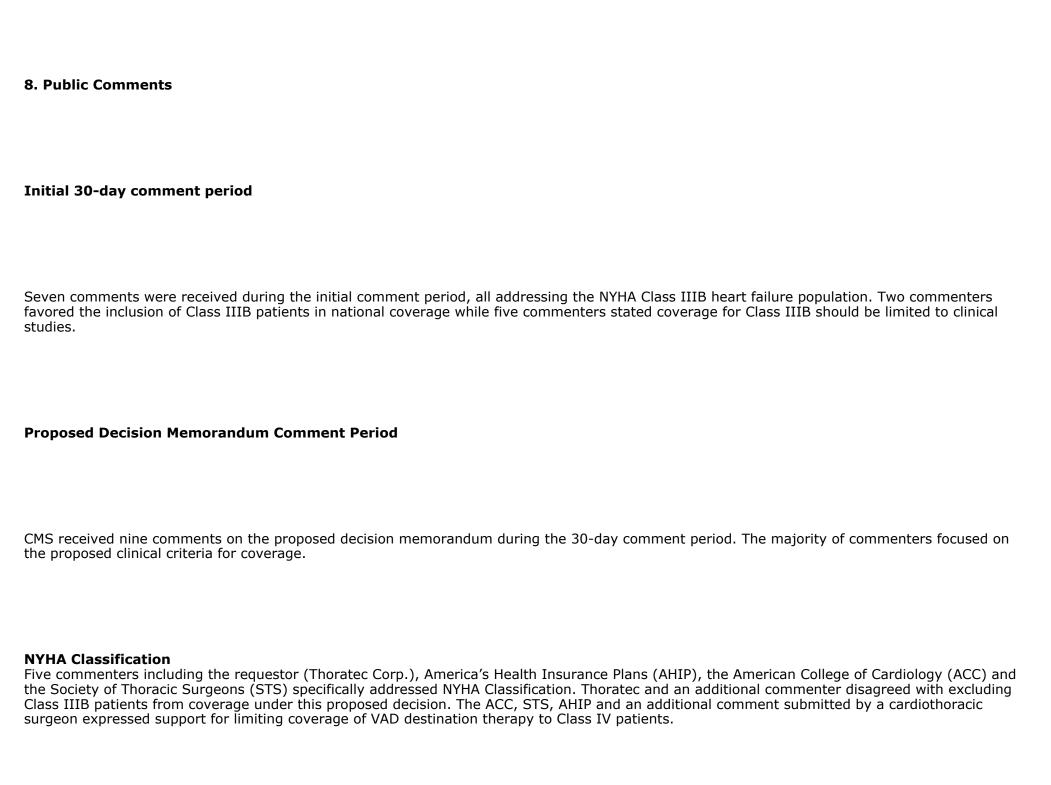
Hunt SA et al. 2009 Focused Update Incorporated Into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults. Circulation. 2009;119:e391-e479.

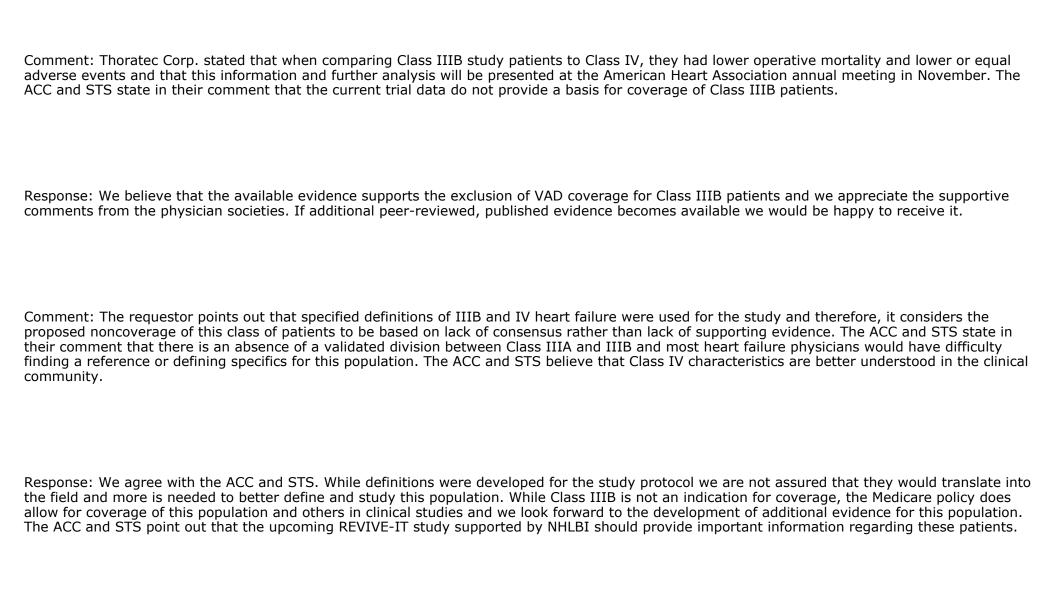
The American College of Cardiology (ACC) and the American Heart Association (AHA) first published guidelines for the evaluation and management of heart failure (HF) in 1995. Those guidelines were updated in 2001 and 2005 and a focused update was published in 2009. The 2001 document introduced a new classification system for describing the development and progression of heart failure. In this four stage system the first two stages (A and B) are designed to provide early identification of patients at risk for developing heart failure. Stage C describes patients with current or past symptoms of heart failure and underlying structural disease (majority of patients). Stage D describes patients with refractory heart failure requiring specialized treatments which may include mechanical circulatory support. This new "classification system is intended to complement but in no way replace the New York Heart Association functional classification, which primarily gauges the severity of symptoms in patients who are in Stage C or D...although symptoms (NYHA class) might vary widely over time (in response to therapy or to progression of disease) in a patient who has already developed the clinical syndrome of HF (Stage C), the patient could never return to stage B (never had HF) ..."

There are no definitions of the NYHA functional classifications included the ACC/AHA Guidelines. The authors note that this classification system "reflects a subjective assessment by a healthcare provider and can change frequently over short periods of time." "A variety of approaches have been used to quantify the degree of functional limitation imposed by HF. The most widely used scale is the NYHA functional classification, but this system is subject to considerable interobserver variability and is insensitive to important changes in exercise capacity... Maximal exercise testing, with measurement of peak oxygen uptake, has been used to identify appropriate candidates for cardiac transplantation, to determine disability, and to assist in the formulation of an exercise prescription, but its role in the general management of patients with HF has not been defined."

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Peak Oxygen Consumption

Comment: Four commenters specifically addressed the requirement of peak oxygen consumption. AHIP and the requestor support the changes from 12 to 14ml/kg. Two commenters stated that the requirement of maximum peak oxygen consumption is not an appropriate measure for patients that are inotrope or balloon pump dependent as these patients may not be capable of performing the tests required to measure peak oxygen.

Response: We have revised the proposed decision and have incorporated broader language to take into account patients that are inotrope dependent
or otherwise not able to physically perform such a test. The coverage requirement will read as follows:

c. have demonstrated functional limitation with a peak oxygen consumption of ≤14 ml/kg/min unless physically unable to perform the test or the test is contra-indicated.

Ejection Fraction

Comment: America's Health Insurance Plans commented that the requirement of a maximum ejection fraction should be removed to allow for flexibility in patient selection. They contend that patients with an EF of 26 and 27 would still benefit from the device.

Response: No data have been presented on the use of ventricular assist devices for destination therapy in patients with EF >25. The results of the REMATCH trial that formed the basis for the first Medicare coverage of destination therapy in 2003 required an EF <25 as did the HeartMate II trial which is the basis for the current decision. Actually, in both trials the EFs of enrolled patients were significantly lower than 25 with the average in both trials being 17. Data from other trials with higher EFs would be needed to consider a change.

Balloon Pump Dependence

Comment: Four commenters responded to the inclusion criteria of 7 day balloon pump dependence. AHIP and the requestor supported the proposed decision. A device manufacturer and a cardiothoracic surgeon provided similar comments. They pointed out that other hemodynamic support devices could be used and are supported for use by the ACC/AHA guidelines for treating Class IV heart failure. They expressed concern that if coverage specifically addresses balloon pump dependency as an indication of coverage then physicians may inappropriately choose this type of device for their patient as opposed to other appropriate, FDA approved devices.

Response: We are not aware of any VAD destination therapy study that has enrolled patients on other hemodynamic support devices and therefore we have not reviewed evidence on this population. The HeartMate II destination study explicitly excluded patients on other ongoing mechanical circulatory support devices. Patients on other mechanical circulatory support are not excluded from Medicare coverage, rather, they would need to qualify based on other criteria.

Comment: Two commenters (a cardiothoracic surgeon and a device manufacturer) were concerned that the proposed policy is worded in a way that would encompass patients who would be eligible for shorter term mechanical circulatory support devices until their native heart is given the opportunity to recover function. One commenter specifically suggests that requiring Class IV heart failure for 90 days prior to implantation would make it clear that this coverage would not apply to recovery patients.

Response: We do not expect this policy to impact care and device selection for recovery patients. The policy language targets destination therapy patients and not those that are likely to recover heart function. Under this policy, coverage is limited to use of the device as an intended permanent therapy, requires chronic heart failure and further, limits coverage for destination therapy to the FDA labeled indication. The patient must also be determined ineligible for transplant which would generally require a thorough review of the patient's condition by heart failure specialists and surgeons. CMS does not have a coverage determination that explicitly applies to acute MI shock patients. The current NCD applies to postcardiotomy patients but simply states that the device used must be approved by the FDA for that purpose.

Due to the other clinical criteria for coverage which restrict the qualifying population, we will not require that patients have Class IV heart failure for 90 days prior to implementation.

Coverage of Equipment at Discharge

Comment: America's Health Insurance Plans commented that CMS should include coverage of the discharge kits associated with these devices. Included in these kits are the items necessary to use the device outside of a hospital setting.

Response: We only addressed patient selection criteria in this decision. However, we expect patients be discharged with all the necessary equipment to successfully operate the device outside the hospital.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1862(I) of the Act.) In order to be covered by Medicare, an item or service must first fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a)(1)(A)of the Act. This section presents the agency's evaluation of the evidence considered and conclusions reached for the assessment.

We address each of the analytic questions below.

Is the evidence adequate to conclude that VADs improve health outcomes of Medicare beneficiaries who are not candidates for transplant and who: a. are said to have NYHA Class IIIB symptoms?

The NYHA classification system was developed in 1928 as a method of describing both the severity and prognosis for heart failure patients. It can also be used to assess response to treatment (Table 3). When last revised in 1994, none of the four classes contained a subclassification. Class III is defined as: "Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or angina pain." Class IV is defined as: "Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the angina syndrome may be present even at rest. If any physical activity is undertaken, discomfort in increased." While its use is long-standing and widespread, the NYHA class is not very reproducible and doesn't reliably predict the walking distance or exercise tolerance on formal testing. Class III includes a number of subjective elements, e.g., "marked limitation," and "less than ordinary activity." The definition of Class IIIb in Chavey et al. (2001), "recent history of dyspnea at rest," differs from the unpublished definition provided by Thoratec. The subclassification IIIB is not widely accepted, does not appear in professional society guidelines or position statements, and appears in few citations in the published peer-reviewed medical literature outside of the Slaughter et al. 2009 and Rogers et al. 2010 articles.

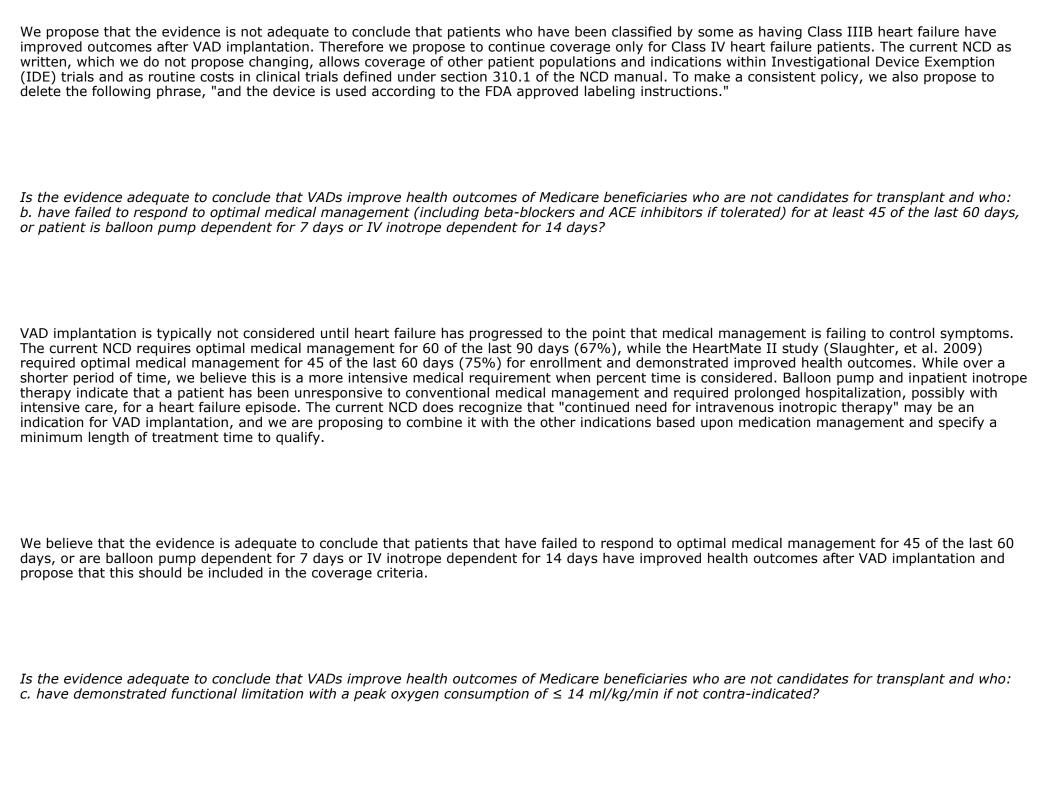
Since 1980 the American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly produced guidelines for the treatment and diagnosis of heart failure. The 2001 update of these guidelines included a new approach to classification of heart failure that emphasized both the development and progression of the disease with definition of four stages. The 2009 update to the guidelines states: "Stage D designates patients with truly refractory HF who might be eligible for specialized, advanced treatment strategies, such as mechanical circulatory support, procedures to facilitate fluid removal, continuous inotropic infusions, or cardiac transplantation..." Stage C "denotes patients with current or past symptoms of HF associated with underlying structural heart disease (the bulk of patients with HF)." Stage D appears most closely related to NYHA Class IV, but Stage C does not appear to describe patients with such advanced disease.

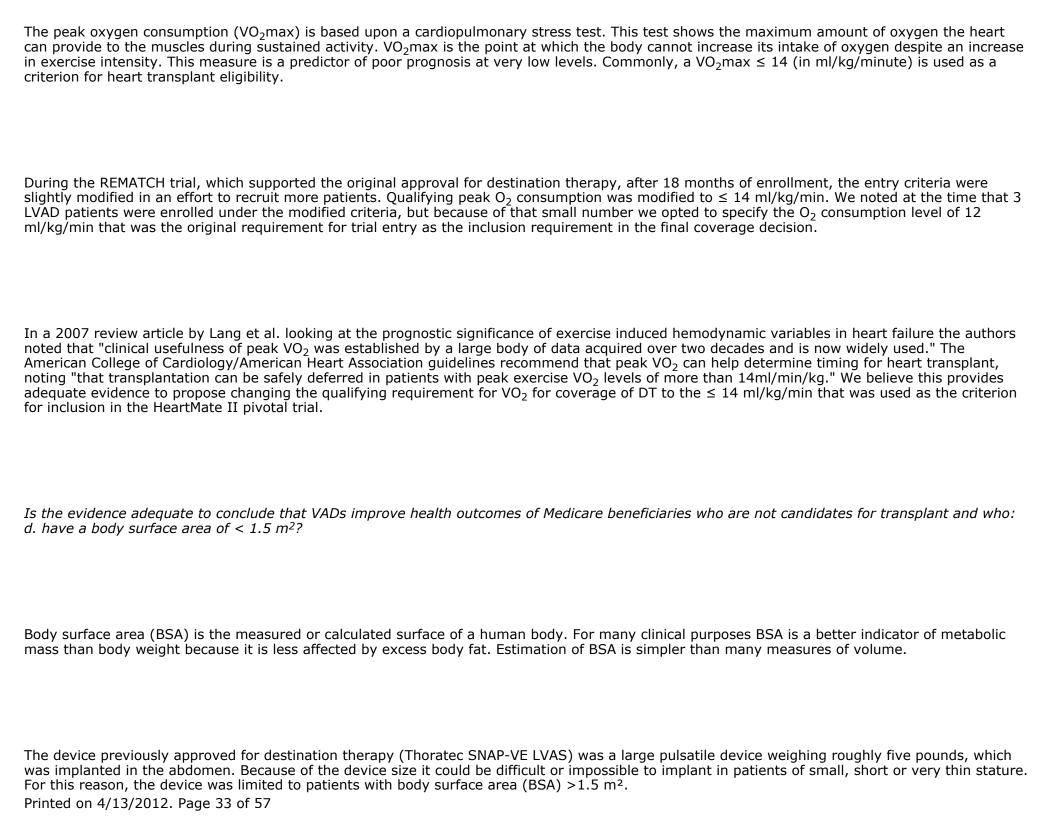
No definition of NYHA Class IIIB was found by CMS in reviewing both the published trial results (Slaughter, et al. 2009) and the FDA's Summary of Safety and Effectiveness

(http://www.accessdata.fda.gov/cdrh_docs/pdf6/P060040S005b.pdf). The study enrolled 31 Class III patients (4 Class IIIA and 27 Class IIIB) in the HeartMate II arm of the study and 12 Class III patients (1 Class IIIA and 11 Class IIIB) in the HeartMate XVE arm. However, neither the published report of the pivotal HeartMate II destination therapy trial nor the supplementary material accompanying it provided information about differences in outcomes between patients in NYHA class III vs. class IV.

We are aware that additional destination therapy patients outside of the pivotal group have been implanted, both as part of a continued access protocol and in several cohort studies; however detailed data by NYHA class for these patients including outcomes and complications have not been published.

While the pivotal study (Slaughter, et al. 2009) achieved overall good outcomes, Class III patients represent only about one-fourth of the enrolled patients. We have significant concern regarding the ability to replicate the study outcomes in the IIIB population outside of the controlled study. We do not believe the classification IIIB is generally accepted. Class IIIB is not a heart failure class that is included in the current ACC/AHA guidelines regarding heart failure and we are not aware that it is a classification commonly in use by heart failure specialists. Therefore, we do not believe it would be possible to identify patients accurately enough to replicate the study's selection criteria in routine clinical practice.





The study by Musci et al. (2008) demonstrates no difference in mortality outcomes after VAD implantation for patients with low BMI compared to normal BMI. Since the correlation between BMI and BSA is about r=0.9, this evidence can be generalized to persons with low body surface area. The HeartMate II is a continuous-flow device weighing approximately one pound. The small size of the HeartMate II permits implantation in a wider variety of body types. Initial data on 10 small BSA patients was analyzed by FDA for this device used for bridge to transplant, without notable adverse events (http://www.accessdata.fda.gov/cdrh_docs/pdf6/P060040b.pdf). In order to gather data on the impact, if any, of reduced body size on patient outcomes a cohort of small body size patients, who could not be randomized in the pivotal trial, was studied and reviewed by FDA. The FDA approval no longer specifies a minimum BSA for implantation. While implanting physicians must determine appropriate fit of the selected device for the individual patient, we propose that the evidence is adequate to remove minimum body surface area from Medicare coverage requirements. Summary The HeartMate II destination therapy study succeeded in meeting the pre-specified endpoints and demonstrated that overall the study subjects that received the HeartMate II device had better health outcomes than patients that received the XVE. The as-treated analysis demonstrates a substantial survival advantage for subjects treated with HeartMate II, with survival of 58% at two years. For comparison purposes the two year results for the primary endpoint of survival in the REMATCH trial was 23% for device recipients and 8 % for medical therapy patients.

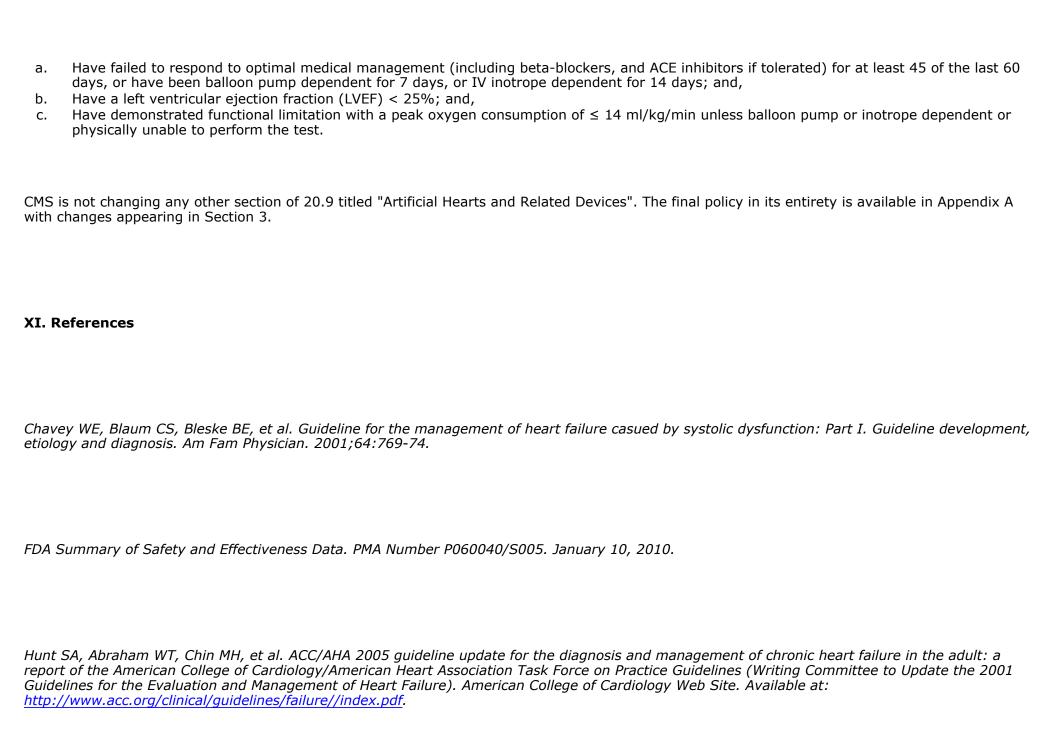
The study protocol was designed to minimize study bias and the results were obtained with adequate data quality. Improvement in device durability and lower risks associated with devices such as shown in the pivotal study are critical to potentially expanding the population of device candidates to a slightly less sick patient population. Because of the relatively high use of inotropes and previously implanted devices most patients could be described by the 2009 ACC/AHA guidelines as Stage D. Risks related to VAD implantation remain significant and therefore should be carefully considered when determining device candidacy. As is the case with many of the clinical studies related to cardiac devices, patient enrollment is primarily comprised of Caucasian men. Minorities are generally underrepresented. As these devices are able to be used in smaller patients, we expect more women to be included in future studies. Studies should also enroll members of other underrepresented populations to better understand the potential for health disparities.

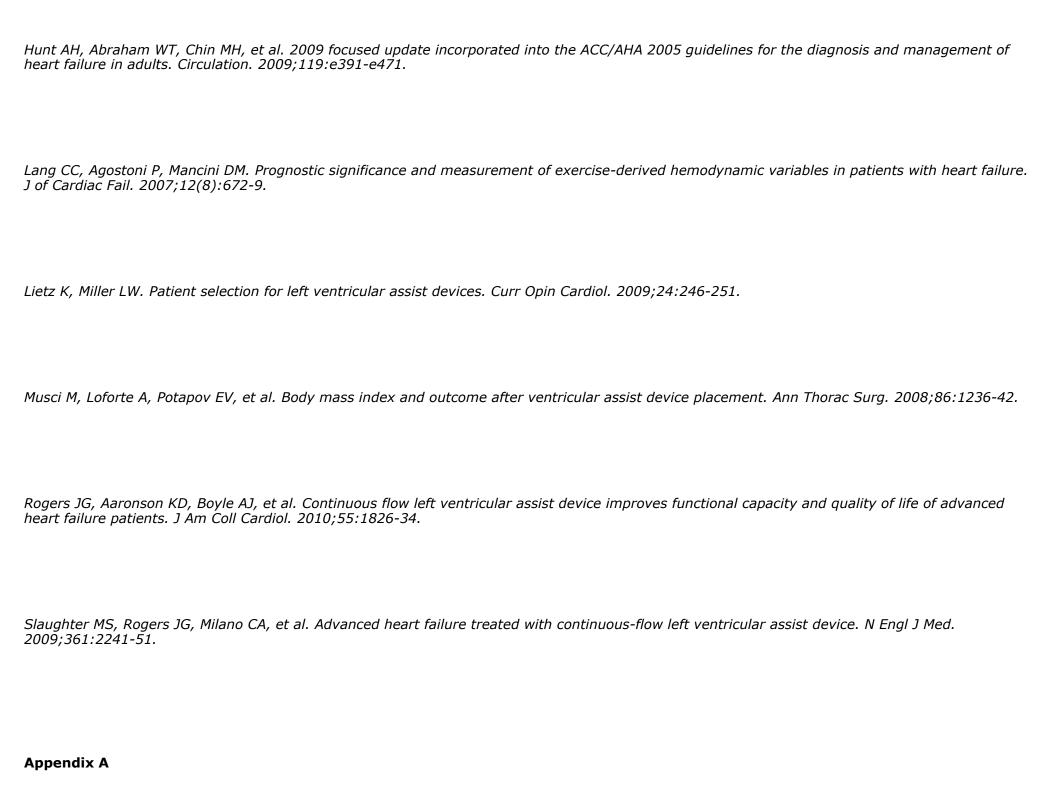
The overall results of the HeartMate II destination therapy pivotal study and additional literature support changing the peak VO $_2$ and body size requirements. VO $_2 \le 14$ ml/kl/min serves as a current standard for transplant and body size requirements have and will continue to change over time as devices become smaller. Our proposal to change the medical management requirement is based on the pivotal study and that while the time on maximal medical management may be lessened by 30 days, the requirement of being treated maximally for 45 of 60 day is perhaps even more intense than the previous requirement. We are not proposing to extend coverage to Class IIIB heart failure patients. While these patients were enrolled in the pivotal study, they are a small portion of the whole group and published evidence is not available regarding their specific outcomes. However, a major consideration is the inability of heart failure specialists to replicate the entry criteria used in the pivotal study. The definition of Class IIIB was specifically for the study and is not generally accepted.

Public comment was generally in agreement with our proposed decision. We have in response to comments revised the proposed decision to address the inability of persons with certain conditions to accomplish peak oxygen consumption testing. In conclusion, we propose to change the requirements for peak VO_2 , medical management and body size.

IX. Conclusion

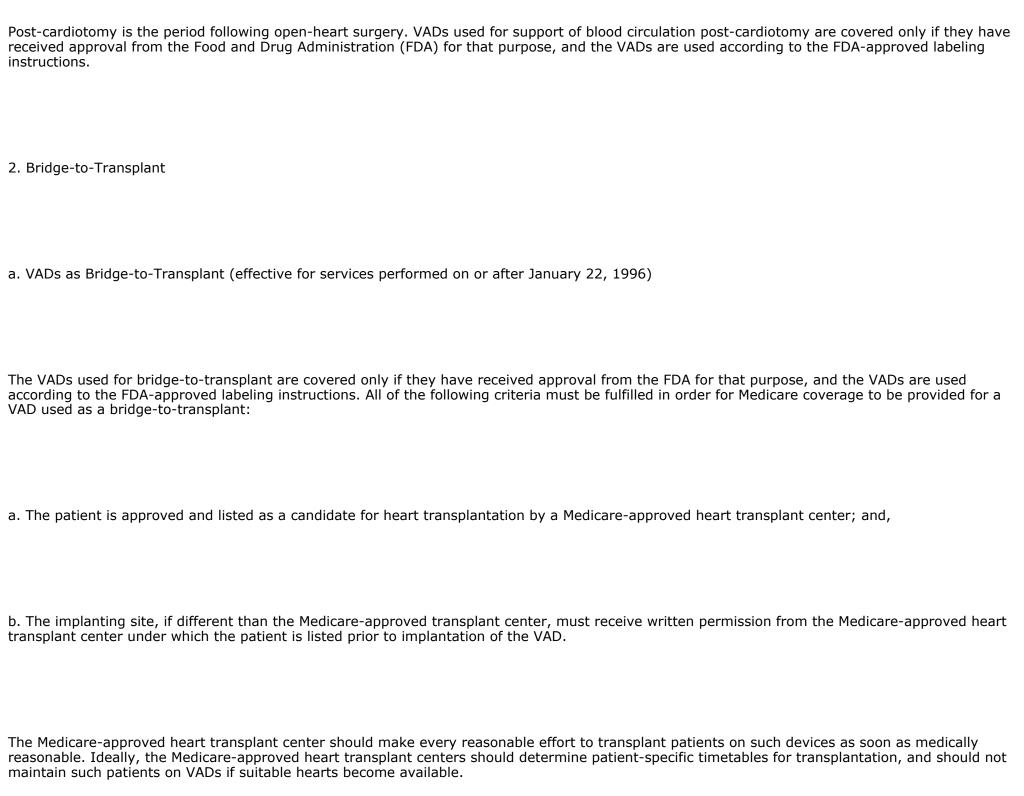
The evidence is adequate to conclude that VAD implantation as destination therapy improves health outcomes and is reasonable and necessary when the device has received FDA approval for a destination therapy indication and only for patients with New York Heart Association (NYHA) Class IV end-stage ventricular heart failure, who are not candidates for heart transplant and who meet all of the following conditions:





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Draft NCD
20.9 - Artificial Hearts And Related Devices (Various Effective Dates Below)
A. General
A ventricular assist device (VAD) or left ventricular assist device (LVAD) is surgically attached to one or both intact ventricles and is used to assist a damaged or weakened native heart in pumping blood. Improvement in the performance of the native heart may allow the device to be removed.
An artificial heart is a biventricular replacement device which requires removal of a substantial part of the native heart, including both ventricles. Removal of this device is not compatible with life, unless the patient has a heart transplant.
Removal of this device is not compatible with life, unless the patient has a heart transplant.
B. Nationally Covered Indications
1. Postcardiotomy (effective for services performed on or after October 18, 1993)



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b. Artificial Heart as Bridge-to-Transplant (effective for services performed on or after May 1, 2008)
An artificial heart for bridge-to-transplantation is covered when performed under coverage with evidence development (CED) when a clinical study meets all of the criteria listed below.
The clinical study must address at least one of the following questions:
 Were there unique circumstances such as expertise available in a particular facility or an unusual combination of conditions in particular patients that affected their outcomes?
• What will be the average time to device failure when the device is made available to larger numbers of patients?
 Do results adequately give a reasonable indication of the full range of outcomes (both positive and negative) that might be expected from more widespread use?

The clinical study must meet all of the following criteria:
• The study must be reviewed and approved by the FDA.
• The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
• The research study is well supported by available scientific and medical information, or it is intended to clarify or establish the health outcomes of nterventions already in common clinical use.
• The research study does not unjustifiably duplicate existing studies.
• The research study design is appropriate to answer the research question being asked in the study.
• The research study is sponsored by an organization or individual capable of executing the proposed study successfully.

• The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is FDA-regulated it also must be in compliance with 21 CFR Parts 50 and 56.
• All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
• The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for coverage with study participation (CSP) or CED coverage.
• The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
• The clinical research study is registered on the ClinicalTrials.gov Web site by the principal sponsor/investigator as demonstrated by having a National Clinical Trial control number.
• The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the international Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later that three (3) years after the end of data collection.

• The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
• The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability, or Medicaid eligibility.
Consistent with section 1142 of the Social Security Act (the Act), the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.
The principal investigator of an artificial heart clinical study seeking Medicare payment should submit the following documentation to the Centers fo Medicare & Medicaid Services (CMS) and should expect to be notified when the CMS review is complete:
• Complete study protocol (must be dated or identified with a version number);
• Protocol summary;

• Statement that the submitted protocol version has been agreed upon by the FDA;
• Statement that the above study standards are met;
• Statement that the study addresses at least one of the above questions related to artificial hearts;
• Complete contact information (phone number, email address, and mailing address); and,
• Clinicaltrials.gov registration number.
The above information should be mailed to: Director, Coverage and Analysis Group Centers for Medicare and Medicaid Services Re: Artificial Heart Mailstop C1-09-06 7500 Security Blvd. Baltimore, MD 21244-1850
Clinical studies that are determined by CMS to meet the above requirements will be listed on the CMS Web site at: http://www.cms.gov/MedicareApprovedFacilitie/06_artificialhearts.asp.

3. I	Destin	ation	The	apy
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a. VADs as Destination Therapy (effective for services performed on or after October 1, 2003, patient selection criteria updated 11/09/2010 and facility criteria updated March 27, 2007)

Destination therapy is for patients that require permanent mechanical cardiac support. The VADs used for destination therapy are covered only if they have received approval from the FDA for that purpose.

Patient Selection

The VADs are covered for patients who have chronic end-stage heart failure (New York Heart Association Class IV end-stage left ventricular failure), who are not candidates for heart transplantation, and meet all of the following conditions:

- a. have failed to respond to optimal medical management (including beta-blockers and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump dependent for 7 days, or IV inotrope dependent for 14 days; and
- b. have a left ventricular ejection fraction (LVEF) <25%;
- c. have demonstrated functional limitation with a peak oxygen consumption of ≤ 14 ml/kg/min unless balloon pump or inotrope dependent or physically unable to perform the test.

Facility Criteria

- a. Facilities must have at least one member of the VAD team with experience implanting at least 10 VADs (as bridge-to-transplant or destination therapy) or artificial hearts over the course of the previous 36 months;
- b. Facilities must be a member of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS); and,
- c. By March 27, 2009, all facilities must meet the above facility criteria and be credentialed by the Joint Commission under the Disease Specific Certification Program for Ventricular Assist Devices (standards dated February 2007).

The Web site http://www.cms.gov/MedicareApprovedFacilitie/VAD/list.asp#TopOfPage will be updated continuously to list all approved facilities. Facilities gaining Joint Commission certification (including prior to March 27, 2009) will be added to the Web site when certification is obtained.
Hospitals also must have in place staff and procedures that ensure that prospective VAD recipients receive all information necessary to assist them in giving appropriate informed consent for the procedure so that they and their families are fully aware of the aftercare requirements and potential limitations, as well as benefits, following VAD implantation.
b. Artificial Heart as Destination Therapy (effective for services performed on or after May 1, 2008)
An artificial heart for destination therapy is covered when performed under CED when a clinical study meets all of the criteria listed below:
The clinical study must address at least one of the following questions:
• Were there unique circumstances such as expertise available in a particular facility or an unusual combination of conditions in particular patients that affected their outcomes?
What will be the average time to device failure when the device is made available to larger numbers of patients?

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Do results adequately give a reasonable indication of the full range of outcomes (both positive and negative) that might be expected from more vide spread use?
The clinical study must meet all of the following criteria:
The study must be reviewed and approved by the FDA.
The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes onterventions already in common clinical use.
The research study does not unjustifiably duplicate existing studies.

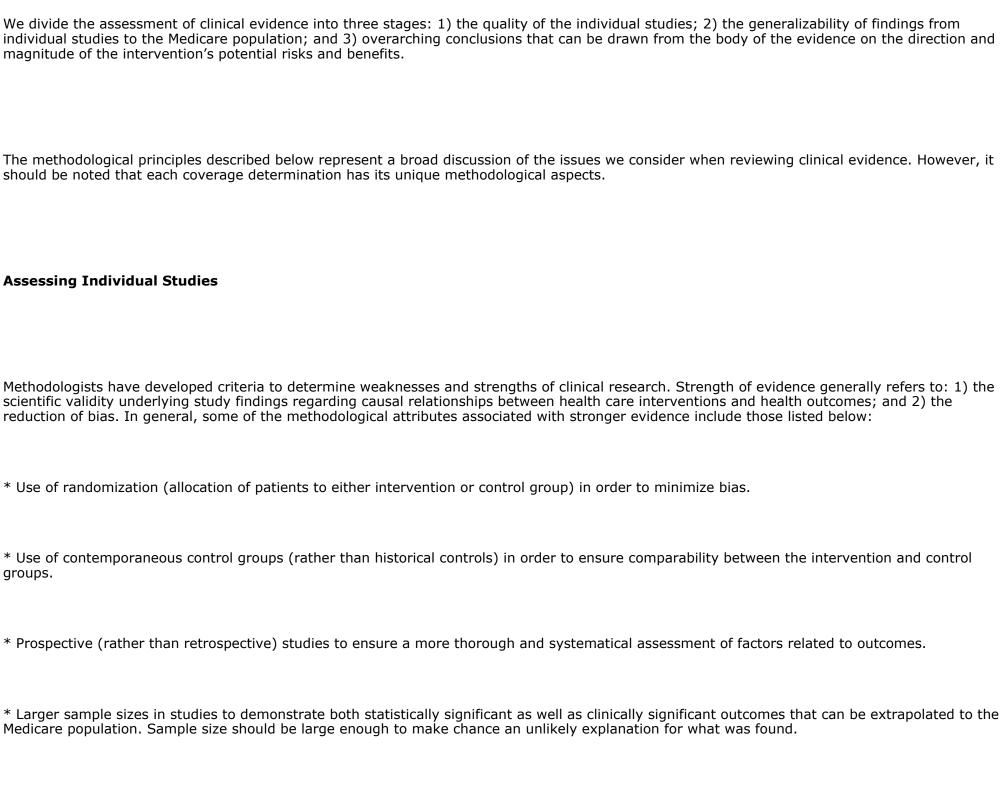
The research study design is appropriate to answer the research question being asked in the study.
The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. a study is FDA-regulated it also must be in compliance with 21 CFR Parts 50 and 56.
All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirement or CSP or CED coverage.
The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical echnologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life hreatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator as demonstrated by having a National Clinical Trial control number.

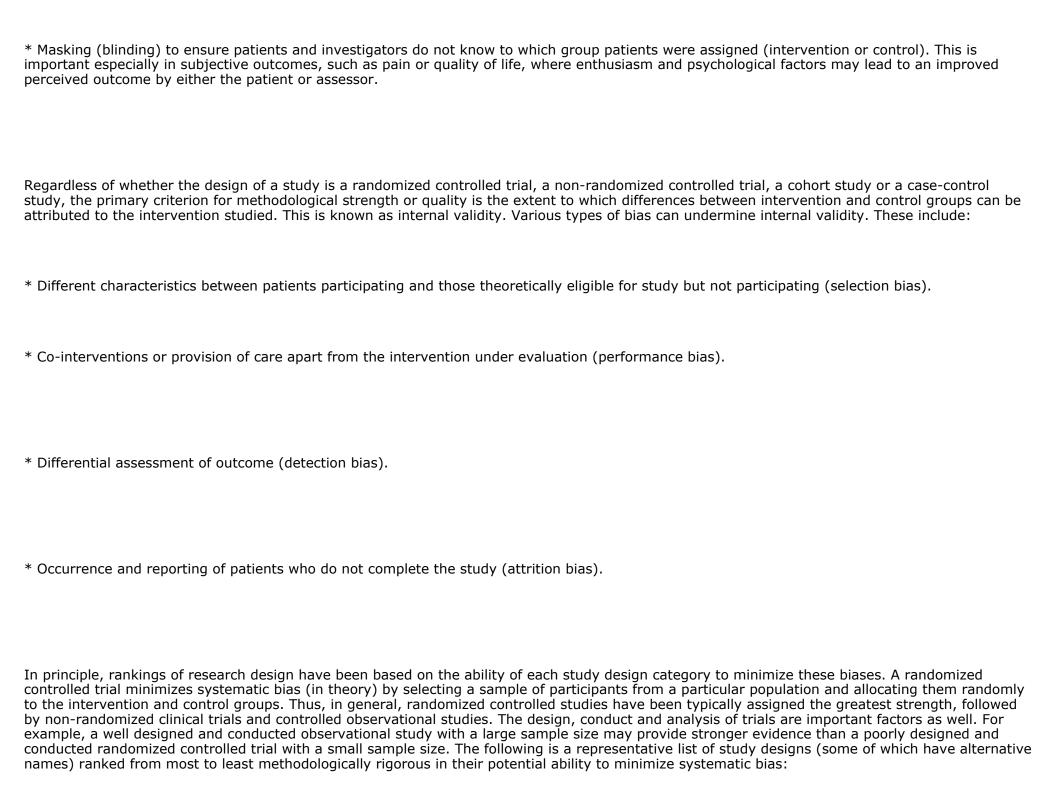
• The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.
• The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
• The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.
Consistent with section 1142 of the Act, AHRQ supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.
The principal investigator of an artificial heart clinical study seeking Medicare payment should submit the following documentation to CMS and should expect to be notified when the CMS review is complete:
• Complete study protocol (must be dated or identified with a version number);

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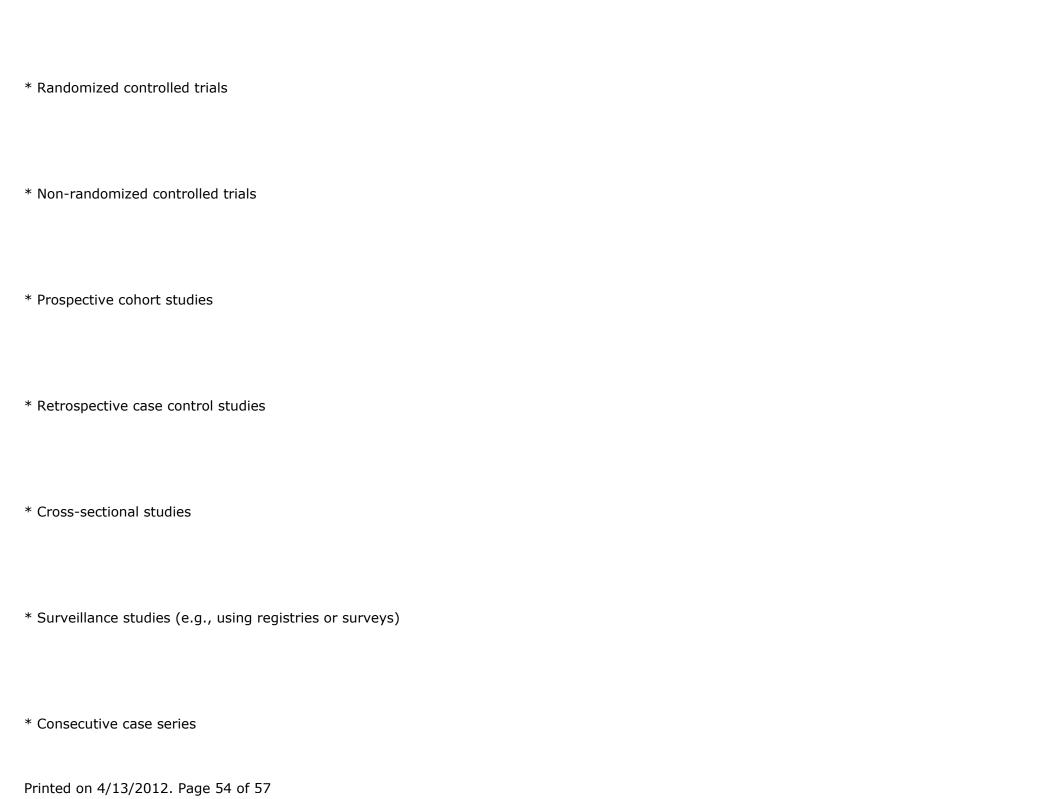
• Protocol summary;
• Statement that the submitted protocol version has been agreed upon by the FDA;
• Statement that the above study standards are met;
• Statement that the study addresses at least one of the above questions related to artificial hearts;
• Complete contact information (phone number, email address and mailing address); and,
Clinicaltrials.gov registration number.
The above information should be mailed to: Director, Coverage and Analysis Group Centers for Medicare and Medicaid Services

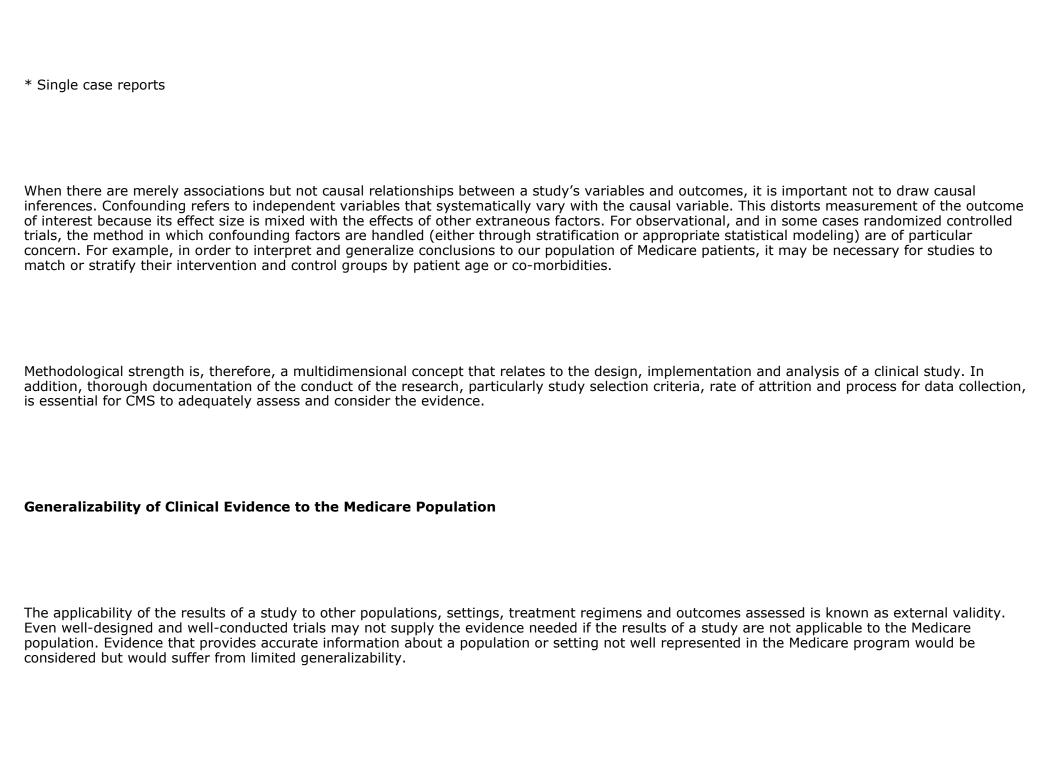
Re: Artificial Heart Mailstop C1-09-06 7500 Security Blvd. Baltimore, MD 21244-1850
Clinical studies that are determined by CMS to meet the above requirements will be listed on the CMS Web site. http://www.cms.gov/MedicareApprovedFacilitie/06_artificialhearts.asp .
C. Nationally Non-Covered Indications (effective for services performed on or after May 19, 1986) All other indications for the use of VADs or artificial hearts not otherwise listed remain non-covered, except in the context of Category B IDE clinical crials (42 CFR 405) or as a routine cost in clinical trials defined under section 310.1 of the NCD Manual.
(This NCD last reviewed April 2008.) Appendix B
General Methodological Principles of Study Design
When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will mprove health outcomes for patients.

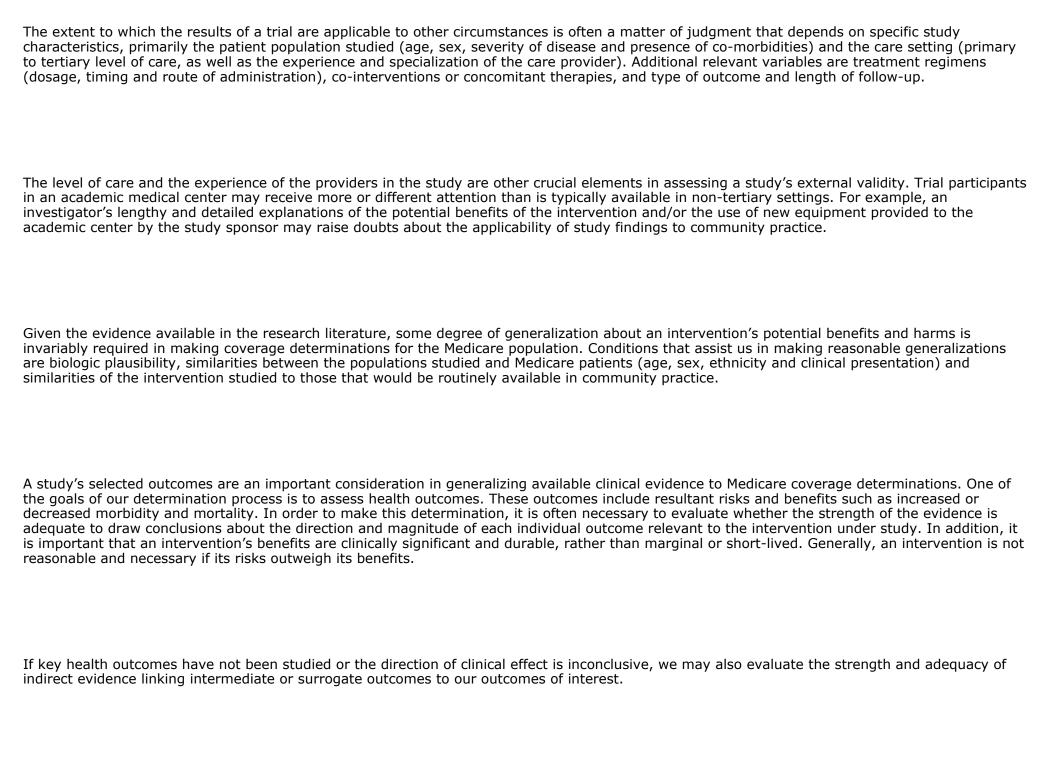




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Assessing the Relative Magnitude of Risks and Benefits Drinted on 4/12/2012, Page 56 of 57

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Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

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